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EDITORIAL

THE CONTROL OF TUBERCULOSIS IN CATTLE

Some interesting and instructive figures were given at the recent Conference of the Royal Sanitary Institute by J. N. Ritchie on the position of attested herds in this country. He showed that there had been considerable progress under the Tuberculosis (Attested Herds) Scheme in recent years. Thus, in Great Britain, at the end of 1947, we had a total of 30,436 attested herds, with 1,199,929 cattle in them, i.e., 13.9 per cent. of the total cattle population. He pointed out that progress had not been equally rapid throughout the country and gave some further figures by way of illustration. The number of attested herds in England was 9,445, with 518,412 cattle or 8.3 per cent. of its total population; in Wales, the number was 11,099, with 229,210 cattle or 25.5 per cent.; in Scotland it was 9,892 herds, with 452,397 cattle or 31 per cent. Some further figures indicate the distribution of these attested herds. Examples of their numbers in counties are given: Zetland has all its cattle in attested herds; Bute, at the end of 1947, had 84 per cent. of its cattle in attested herds; Ayr had 79 per cent.; Cardigan had 72.5 per cent.; Carmarthen had 64.6 per cent.; Dumfries had 61.6 per cent. There were four counties in Scotland with 50-60 per cent.; four counties in Scotland, two in Wales and one in England with 30-50 per cent.; five in Scotland and two in England had 20-30 per cent. In addition to cattle in attested herds, there were approximately 250,000 cattle in herds not attested but licensed to produce T.T. milk. This information is decidedly encouraging and speaks well for the effort in controlling tuberculosis by the measures at present in operation. It also shows that the tuberculin test as carried out in recent years is reliable and yields satisfactory results. All this work has been the result of co-operation between the veterinary profession and the farming community and is an example of what can be done. We will expect further efforts in the future.

GENERAL ARTICLES

THE BIOCHEMICAL APPROACH TO ANIMAL DISEASE

The Fison Lectures, 1948, of the Animal Health Trust

By PROFESSOR L. SEEKLES, D.Sc.
Utrecht University

II—Gastro-Intestinal Autointoxication in Cattle and Horses

Introduction

Nobody will deny the vital importance of the chemical composition and the colloid-chemical structure of food with regard to the origin of disease. But there is still another factor of no less importance: the action of the animal on the food administered. It is not exclusively the chemical composition and the colloidal structure of the food which determine its biological value and digestibility. Probably there exists a specific arrangement of the cells of the intestine and other organs concerning the absorption and metabolism of food components. The processes of absorption and metabolism of normal and abnormal food are dependent on the *vital capacity* of the cells of the animal body.

Moreover, the metabolic processes of several components of the food have been shown to be inter-related. *"Conditioned deficiencies"* and *"conditioned intoxications"* may arise even in cases in which neither real deficiencies nor toxic substances are present in the food.

So the origin of metabolic disturbances in relation to food may be fundamentally based on the histo-chemical arrangement of the animal tissues which determines their biochemical potency with respect to the progress of metabolism.

This lecture deals with some aspects of the work performed in my laboratory in recent years, firstly concerning gastro-intestinal disturbances following the ingestion of food of normal or nearly normal composition.

Abnormal activity of the animal on the food may originate in three ways: 1° from abnormal chemical reactions in the gastro-intestinal tract previous to absorption, 2° from an abnormal absorption of scission products of food components, and 3° from abnormal metabolic processes of substances after they have been absorbed and passed into the animal tissues.

Knowledge of these three phenomena deepens our insight into the origin of disease and opens the way to a rational prophylaxis and therapy.

Biochemical Nature of Gastro-Intestinal Disturbances

In cases of the *normal functioning* of the gastro-intestinal tract small quantities of toxic substances, such as phenols, amines, ammonia, indol, scatol, etc., are formed in the intestine. They are partly removed by excretion in the fæces, and partly absorbed and carried by the portal vein to the liver. Detoxication occurs in three ways:

1° by coupling of the poisonous substance with other substances of non-toxic

character. In this way *lipophilic* substances which may penetrate into the cells may be converted into *hydrophilic* substances which may be easily excreted by the kidneys;

2° by oxidation under the influence of several enzymatic systems which often contain minor elements as essential constituents of the enzyme molecule or which may require activation by ions of minor elements,[1] or

3° by deposition in various tissues.

The normal state of the animal body is characterised by an *"intoxication-detoxication" balance,* in which the detoxication-reactions keep step with the intoxication-reactions.

In cases of *abnormal functioning* of the gastro-intestinal tract, however, an increased absorption of these toxic substances may occur.[2]

They may arise in considerable quantities as a result of abnormal fermentations and other similar biochemical changes of the partially digested food. They may arise from the phenomenon of *"dysbacteria,"* that is to say an abnormal bacteriological action in the intestine which may be due to a migration of (normal) intestinal bacteria to abnormal areas in the intestinal tract. Or they may arise from inflammatory changes of the intestinal wall. Intestinal stasis involving decreased rate of excretion may facilitate absorption of toxic substances. If the intoxication surpasses the normally occurring detoxication reactions of the animal body biochemical and clinical features of "autointoxication" may develop to a varying extent, dependent on the shift of the normally existing "intoxication-detoxication equilibrium."

It should be emphasised that toxic substances of various kinds originating from other parts of the animal body probably may act in a similar way, e.g., substances originating from necrotic changes of subcutaneous tissue following injections of hypertonic solutions,[3] from bacteriological processes in different organs, or from the secretion of excessive quantities of hormones. According to observations in my laboratory "hormonal intoxication" may be a factor in milk fever[4] and in related syndromes, e.g., acute acetonæmia.

The different possibilities from which (auto)-intoxication originates may be summarised as follows:—

A. Increased Intoxication

I Poisons of exogenic origin. (This cause may be excluded in cases of *auto*-intoxication.)

II Migration of intestinal bacteria to abnormal places in the intestinal tract, called "Dysbacteria,"

1. originating from sudden changes of the food, e.g., on removing the animals from the byre to pasture;
2. originating from climatic influences, e.g., warm days followed by cold nights;
3. originating from hormonal dysfunction or abnormal supply of vitamins. (In these cases 1, 2 and 3 *disturbances of intestinal motility* followed by intestinal stasis, anti-peristaltic and increased peristaltic movements

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may play an important part. Further: influence of intestinal parasites.)

III Abnormal scission of proteins:
1. originating from the food ("food intoxication");
2. originating from infectious diseases, e.g., endometritis following retention of the placenta (bacteriotoxins").

IV Substances originating from non-protein constituents of the food, e.g. (butyric) acid.

V Changes of the intestinal wall following inflammatory and necrotic processes, followed by abnormal absorption of toxic substances and water on account of altered permeability.

B. Decreased Detoxication

I Inactivation of detoxifying enzyme systems following chemical changes of the medium: pH, oxidation-reduction potential, absence of metals essential to detoxifying enzymes, presence of specific toxins.

II Functional and morphological damage of the liver and other detoxifying organs originating from an abundance of toxic substances.

It is especially the intestine and the liver which are closely related to the origin of autointoxication phenomena.

Moreover, the circulating poisons will affect several other tissues and organs and they will thus, among other things, cause considerable changes in the permeability of the capillary walls and other interfaces. This also renders possible the migration of chemical matter including water which may cause symptoms of medical shock by dehydration. The simultaneous action of several of these factors mentioned in the scheme may cause a considerable variety of biochemical and clinical features, which causes serious difficulties concerning diagnosis. The latter point which is of great importance to practitioners must be examined in greater detail.

Clinical Features of Autointoxication

Several disorders in large domestic animals may be connected in a natural way with dysfunctions of the gastro-intestinal tract. We should like to mention among other things various forms of "indigestion" and "food intoxication"—following the intake of food of *normal* or *nearly normal* composition—in horses and cattle. For example, in cattle the gastro-intestinal form of foot-and-mouth disease, grass tetany and *"longjacht"* (acute emphysema of the lungs) which occurs in the Netherlands when cattle are put to a new pasture in the after-season; in horses the gastro-intestinal form of founder (*pododermatitis diffusa, acuta vel chronica*), grass disease and perhaps moon-blindness (*ophtalmia periodica*). In such cases a careful anamnesis may be extremely useful.

After what has been mentioned above it will be clear that there need not be a deviation in the quantitative and qualitative composition of the food. After all, the occurrence, if any, of autointoxication symptoms is defined by the way the animal reacts upon the administered food.

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Especially in horses and in a lesser degree also in cattle, it is the great sensitiveness of these animals to the development of disorders of the motility of the intestine under the influence of stimuli of an external or internal nature which is the immediate cause of gastro-intestinal disturbances. This condition may be considerably complicated by parasitic and infectious affections of the stomach and intestinal tract. We observe this, e.g., in gastro-intestinal strongylosis, paratuberculosis and the toxic form of foot-and-mouth disease. A complex of clinical symptoms, which manifest themselves in a variable manner, causes the clinical picture of the disease to be very complicated. We would mention: intestinal obstruction, constipation, diarrhœa and "indigestion," (hæmorrhagic) enteritis, jaundice, hæmoglobinuria, methæmoglobinuria, paresis, staggering gate, tetany, excitation, sopor, a frequent pulse rate, a high temperature, rough coats, decreased ingestion of food, symptoms of dehydration (medical shock) and emaciation.

It is the overburdening of the detoxifying organs, especially the liver, which in many cases results in a sudden fall in their detoxifying functions, thus contributing to an avalanche-like increase of the morbid symptoms.

Biochemical Features of Autointoxication

In cases of autointoxication, interference with the *autonomic nervous system* has to be taken into consideration. This implicates disturbances of several metabolic processes dependent upon the autonomic nervous system causing changes of the chemical composition, both organic and inorganic, of the blood and body tissues.[8]

Cattle suffering from the gastro-intestinal form of foot-and-mouth disease showed a decrease in the average value of calcium, a slight decrease of the average value of magnesium and an increase of the average value of inorganic phosphorus of the blood serum.

Considerable variation in individual values of these minerals as well as in values for residual nitrogen, chlorine and cholesterol were found. This is in accordance with the general nature of autointoxication phenomena, i.e., considerable differences in the "intoxication-detoxication rate" in different individuals. However, there is an important point of similarity in the majority of cases observed. The calcium-phosphorus-magnesium triangular graph shows, besides the variations mentioned above, that *in 29 cases out of 32 the proportion between these elements is shifted in favour of inorganic phosphorus* (*Fig.* 1).

In 66 cases of autointoxications and "indigestions" of different origin in cattle listed up to 1939, blood serum values of calcium, magnesium and inorganic phosphorus showed similar and even more considerable variations.[2] The calcium-phosphorus-magnesium triangular graph revealed a close relation between the mineral composition of blood serum in the intestinal form of foot-and-mouth disease and that in cases of autointoxications and indigestions of different origin, progressing with intestinal troubles and as a rule with paresis, tetany and the related symptoms mentioned above. From 66 of these points 53 points were shown

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to occupy the same graphical areas as that characteristic for the gastro-intestinal form of foot-and-mouth disease (Fig. 2).

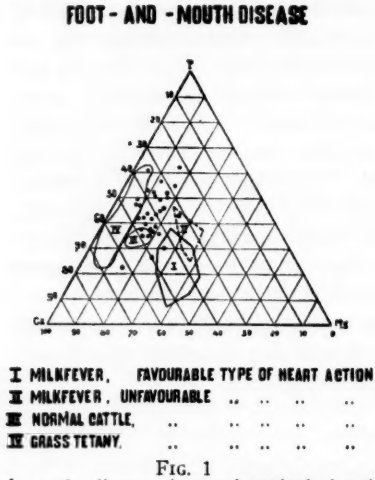
FOOT - AND - MOUTH DISEASE
I MILKFEVER, FAVOURABLE TYPE OF HEART ACTION
II MILKFEVER, UNFAVOURABLE .. ..
III NORMAL CATTLE, ...
IV GRASS TETANY, ...

FIG. 1

Foot-and-mouth disease (gastro-intestinal form). The graphical area of the different points should be compared with the areas concerning heart action observed in other conditions following intravenous injection of calcium salts:

I Milk fever, favourable heart action.
II Milk fever, unfavourable heart action.
III Normal cattle, as a rule unfavourable heart action.
IV Grass tetany, unfavourable heart action.

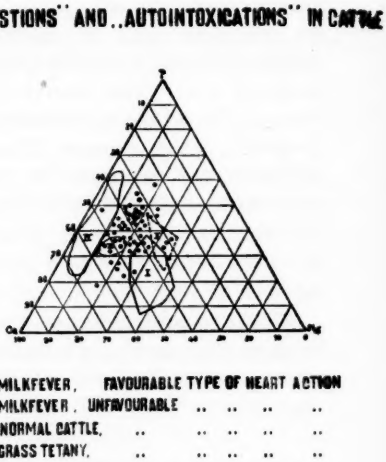
. INDIGESTIONS" AND .. AUTOINTOXICATIONS" IN CATTLE
I MILKFEVER, FAVOURABLE TYPE OF HEART ACTION
II MILKFEVER, UNFAVOURABLE .. ..
III NORMAL CATTLE, ...
IV GRASS TETANY, ...

FIG. 2

"Indigestions" and "Autointoxications." The areas I, II, III, IV are similar to Fig. 1.

A great number of observations listed in recent years were shown to be in accordance with the results mentioned in Fig. 2.

The relation between the mineral shift and the pathogenesis of cardiac disturbance following intravenous injection of calcium salts will be discussed below.

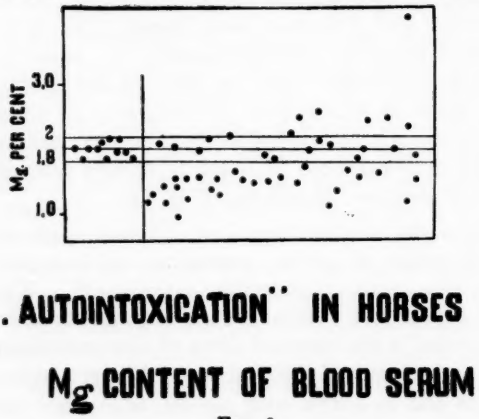

FIG. 3

Hypomagnesemia in horses.

In horses disturbances of the mineral balance of the blood serum was found to be most important concerning the values of magnesium, showing a hypomagnesemia in 60-70 per cent. of the cases observed. Fig. 3 shows the results of some of those cases (48 of which 27 showed a decrease).

Moreover, in horses disturbances of the sugar metabolism causing high values of blood sugar often occur.

" Conditioned Deficiency " and " Conditioned Intoxication "

In most cases it is very difficult to distinguish between the cause and the result of a disordered absorption and a disordered metabolism. Thus, symptoms of pica may arise in cattle *without our being able to connect them with the intake of abnormal food.* In such cases the capacity of the animal to ingest and digest food in the normal manner is nevertheless decreased. This causes a considerable decrease of the net energy from which the body benefits. The animals decline and ultimately they die from exhaustion.

Observation of these kinds of disturbances which are found in different areas in the Netherlands have induced us to introduce the idea of: *" conditioned deficiency,"* e.g., of minor elements, and *" conditioned intoxication."* With these expressions we are alluding to a condition in which the ingestion and digestion of a certain food component, e.g., copper evidently depends on its relation to other components of the food and in general on the reaction of the intestine on the food administered. In these cases changes of the composition of the blood and other tissues may occur.

The idea " conditioned deficiency " is also known in plants. It will be remembered that the copper-supply of a plant should keep step with the metabolism of protein. In case of a rise of the protein conversion, the plant will need more copper to be able to grow normally.

Another example of reciprocal affection of food components which has been known for some time is alkali disease due to a chronic selenium poisoning. This poisoning apparently only shows when we have a diet poor in protein and rich in carbohydrates, such as is given to the larger domestic animals. People living on a diet rich in protein are not subject to trouble from food containing selenium. Here once more we are struck by the connection between the gastro-intestinal tract and the liver. Damage to the mucous membrane of the stomach which may even develop to ulceration is found in addition to degenerative changes in the liver.

Apparently a part is played here by a shortage of the essential amino-acid methionine containing sulphur which in all probability is converted into the selenium-derivative by the selenium which is to be found in the food. However, this latter cannot take over the physiological function of methionine. Administration of food containing methionine, i.e., food rich in protein compensates for the relative shortage of methionine and consequently causes the symptoms of alkali disease including the degeneration of the liver to disappear. As the disorder does not occur in the Netherlands no personal observations are available.

A third example of " conditioned intoxication " together with a " conditioned deficiency " we have found in recent years in cattle suffering from an alimentary form of acetonemia. According to the seriousness of the disturbance these animals may be clinically normal or not. However, in all cases—even in the slightest—a fall in milk production is perceived as well as the occurrence of toxic products, viz., acetone-bodies in the body fluids. This form of alimentary ketosis occurs, e.g., when grass-silage containing much butyric acid is used as a fodder. Yet butyric acid in small quantities is a normal food component which is always formed in the paunch from carbohydrates. Apparently butyric acid absorbed in abnormal

quantities gives rise to the formation of ketone bodies by an impaired oxidation capacity of the liver.

By way of example I would mention the chemical composition of a typical ketogenic silage and of a normal one.

	Ketogenic	*Normal*
(Fresh matter basis)		
Lactic acid	0 per cent. ...	1.25 per cent.
Total acetic acid ...	0.45 „ „ ...	0.14 „ „
Total butyric acid ...	1.81 „ „ ...	0.07 „ „
pH value	5.4 „ „ ...	4.0 „ „
(Dry matter basis)		
Total protein	10 „ „ ...	16.3 „ „
Digestible protein ...	5.2 „ „ ...	9.3 „ „
Crude fibre	40.6 „ „ ...	32.9 „ „

Administering lactate to these patients—also a normal product of fermentation of the contents of the paunch—apparently makes up for the relative lack of this substance. It causes the symptoms of ketosis to disappear, including the fatty infiltration and degeneration of the liver, while the milk production rises.

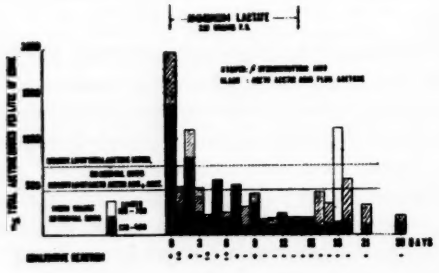

FIG. 4
The treatment of a case of persistent acetonemia in a cow by means of ammonium lactate.

In the course of years a considerable experience has been gained in the Netherlands concerning the treatment of acetonemia in cattle. This includes the typical form of acetonemia occurring about two weeks after parturition which is to all appearance of hormonal origin, as well as different forms of alimentary ketosis occurring in the byre and at pasture.

About a quarter of a century ago a treatment of the typical form of acetonemia by means of dextrose and insulin was introduced by Sjollema. Satisfactory results were recorded in numerous cases. However, in recent years this method could not be applied because of lack of sugar and insulin.

Treatment of acetonemia by means of arsenic, chloral hydrate and potassium chlorate was often practised. It is especially the latter drug which has drawn a good deal of attention in recent years, although its mode of action is still far from being clear. In many cases a treatment with potassium chlorate brought about a rapid cure. However, in several other cases the animals treated were shown to become rapidly worse.

Evidence has been obtained that the result of the potassium chlorate therapy is highly dependent upon the state of the diseased animal. In cases in which the liver function is not seriously damaged, potassium chlorate may act beneficially. Ammonium lactate is administered by mouth in quantities of about 100 grams

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twice a day. The drug has to be diluted with about half a litre of water prior to administration or it may be mixed with other materials and pressed to cakes. As a rule the strength of commercial ammonium lactate is about 80 per cent.

However, in the case of a serious impairment of the liver, potassium chlorate —which after all is a poison to the cells—apparently causes an even more serious damage of this organ.

It should be borne in mind that all these methods are directed to the disappearance of the biochemical symptom of ketonæmia, that is to say, mainly to an improvement of liver function with regard to the oxidation of ketone bodies. However, in cases of mixed intoxication the disappearance of ketone bodies will not remove all clinical features of disease. This is true, for example, in cases of coprostasis in which gastro-intestinal autointoxication caused by scission products of proteins may play an important part. For this reason, in these cases, therapy should also be directed to the symptom of coprostasis. Administration of a laxative has proved to be advisable here.

These facts led us to the lactate therapy. The basis of this therapy is a physiological one. The method is based on two observations:

1. The normal functioning of the liver is mainly dependent upon a normal ratio of glycogen and fat. In cases of impairment of liver function the content of glycogen falls and the content of fat increases.
2. In normal ruminants a synthesis of glycogen is largely brought about by conversion of lactate originating from the gastro-intestinal tract and from muscular actions.

   (Sugars absorbed from the intestine may also play a part in the synthesis of glycogen.)

So it might be expected that in cases of impairment of liver function a supply of lactate to the liver would raise the glycogen content and in this way improve its function.

Since 1942 the lactate therapy has been practised in numerous cases, as a rule with good result. The drug acts less rapidly than potassium chlorate but it has the advantage of being a physiological substance without any poisonous action when administered in normal quantities. Moreover, it has a weakly laxative action, so it acts favourably in cases showing coprostasis.

Evidence has been obtained that in several other conditions of autointoxication in cattle and horses coinciding with fatty infiltration and degeneration of the liver the administration of lactate may act beneficially. The biochemical picture of these disorders is not quite similar in cattle and horses. In cattle ketone bodies appear in the blood in these conditions; in horses there seems to be a production of bile pigment.

Further experiments are running in my laboratory to establish whether other lipotropic substances may be acting in a way similar to lactate.

The Nature of the Toxic Substances in Cases of Autointoxication

In severe cases of autointoxication, i.e., originating from intestinal obstruction, there has been much discussion concerning the participation of a toxic substance

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in the production of the clinical manifestations of shock by dehydration of tissues. Indeed, in men, substances with histamine-like actions seem to have been isolated from damaged loops of gut.[6] These substances may cause capillary dilatation and an increased permeability of the vessels. A loss of blood plasma may provoke a disparity between the circulating blood volume and the vascular bed.

Knowing this, it goes without saying that it was thought to be desirable to undertake an investigation concerning the level of histamine and histamine-like substances in cases of gastro-intestinal autointoxication.

Table I shows the results recently recorded.[7]

TABLE I. HISTAMINE IN BLOOD

	Number of Animals	Number of Determinations	Histamine in blood		Number of values decreased	Number of values increased
			Average value	Limits of variation		
			γ per cent.	γ per cent.		
Cattle normal*	32	37	7.6±s.d.3.3	2.0—15.0	—	—
Cattle, gastro-intest. intoxication	13	15	—	0—20.0	5	1
Horses normal, not in foal	21	21	4.1±s.d.2.0	1.6— 8.0	—	—
Horses, founder of gastro-intest. origin	10	10	—	1.5—12.2	1	2
Horses, gastro-intest. intoxication	31	36	—	0—11	13	5

* In cattle pregnancy has no influence on the histamine content of the blood. In horses there seems to be an increase of the histamine values in the blood during pregnancy.

Table I shows that the spreading of the histamine values is greater in animals suffering from autointoxication than in normal animals. In about 30 per cent. of the cases observed a lowering of these values has been shown to exist, indicating a disappearance of histamine from the blood either by migration through the capillary walls or by destruction in the vascular bed. Increases of the histamine content were shown to occur less frequently than decreases. Evidence has been obtained that the lowering of the content of histamine in the blood gives rise to an unfavourable prognosis, especially in horses

In about 50 per cent. of the cases observed no abnormal histamine values occur. However, it should be emphasised that besides histamine and histamine-like substances other poisons may play a part in the origin of the clinical and biochemical features of autointoxication.

Prophylaxis and Therapy in Cases of Gastro-Intestinal Autointoxication Except Ketonæmia

The observation of disturbances of intestinal movement initiated by stimuli of internal and external origin offers a basis for a rational *phophylaxis* in several cases. When autointoxication is due to feeding large amounts of concentrates or silage (" food intoxication "), withdrawal of the food may act beneficially: con-

centrates as used in field cases in cattle in this laboratory : mixed meals principally containing corn, peanut meal and wheat gluten and grass silage of the butyric acid type. In another experiment in which soya meal was fed to a heifer, no change in the mineral composition of blood serum was observed.

When autointoxication is due to feeding young grass rich in protein and potassium nitrate, as often occurs in spring in the period of grass tetany, an addition of hay or even straw—which are eagerly eaten—was found to be beneficial. Protecting the animals against the influences of too high a temperature and too much sunshine during the days and of low temperatures and cold winds during the nights is thought to be advisable.

Animals out at grass in orchards in the after-season occasionally eat unripe fruits in large amounts. They should be turned to other pastures on days when large amounts of fruits have fallen from the trees.

Similar observations have been made in horses. Feeding freshly harvested cereals will often initiate symptoms of founder. The same thing may occur under the influence of windy and wet weather and following a long tiresome journey on a stony road. The intake of clover and vetch rich in protein may provoke symptoms of gastro-intestinal autointoxication.

In the course of recent years different *therapies* based on the biochemical features of autointoxication mentioned and on the nature of the toxic substances produced have been tried in this laboratory. We mentioned already the control of alimentary ketosis and in general the control of impaired liver function by means of ammonium lactate.

1. From experiments carried out in this laboratory many years ago concerning intravenous calcium therapy in cattle suffering from paresis (milk fever) and (grass) tetany a relation has been established between the mineral composition of blood serum and the behaviour of the heart following intravenous injection of calcium salts.[8] [2]
   The calcium-magnesium therapy was based on these observations. Figs. 2 and 3 show that in the majority of cases of gastro-intestinal autointoxication—in which paresis and tetany may belong to the clinical features—the mineral balance of the blood plasma is *even more unfavourable* than in the " unfavourable " cases of milk fever and grass tetany. These blood data indicate that, as a rule, the " unfavourable " type of cardiac frequency curve of the heart following intravenous injection of calcium salts is to be expected in the type of case mentioned in this paper. This is in accordance with the practitioners' experience and for that reason this treatment is not advisable. As a rule subcutaneous administration of calicum borogluconate or sodium calcium borogluconate[10] and mammary insufflation, though often tried, did not give any permanent success.
2. Starting from the observation on hypomagnesemia, treatment of horses and cattle suffering from autointoxication was tried and met with a moderate, and in several cases, with a striking success. If necessary this treatment—a subcutaneous injection of 30 grams of crystallised magnesium chloride in a 10 per cent. sterile solution—may be repeated on several subsequent days.

Probably part of the beneficial action of magnesium has to be attributed to a lowering of the irritability of several vital tissues and organs by magnesium ions, in this way alleviating reflex nervous mechanisms initiated by toxic substances.

3. A causal therapy has been tried in two ways both based on the increase of oxidation rate of toxic substances especially histamine in the circulation or fixed in the tissues.
   a. From numerous *in vitro* experiments using the diamino-oxydase enzyme which oxidises histamine and other "diamines," it is concluded that of the minor elements observed it is cobalt which acts like an activator. However, the active concentration of cobalt was shown to be rather high in a homogenous solution of blood serum. A concentration of 2.5 mg. per cent. of cobalt caused the oxidation rate of histamine and cadaverine to increase to about 25 per cent. Seven mg. per cent. of cobalt caused an increase of 60 per cent. On account of the fixation ability of histamine and similar substances to animal tissues it seems possible that *in vivo* a treatment with smaller quantities of cobalt may facilitate oxidation of "diamines" fixed by interfaces in the animal body. Further experiments are progressing.
   b. Much more success can be recorded from the addition of a suitable redox-catalyser showing a E_o value adapted to the animal tissues. In several cases of autointoxication in horses—however, not in all cases observed—intravenous administration of 4 grams of methylene blue in a 2 per cent. sterile solution exhibited a remarkable result. If necessary the injection has to be repeated on two or three subsequent days.

Discussion

Owing to abnormal processes in the intestine, disturbances of the absorption of nutrients and unusual metabolic processes in the animal's tissues, a condition of autointoxication ("conditioned intoxication") may arise. This observation may be taken as a starting point for a better insight into the pathogenesis of those diseases which have often been related to the food. Stimuli of internal and external origin such as toxic substances produced in the intestine (or in other organs), sudden changes of the food, overburdening of the gastro-intestinal tract, hormonal dysfunctions and climatic factors may initiate disturbances of intestinal motility. This may originate the abnormal processes mentioned above. A rational prophylaxis has to be based on this observation.

Gastro-intestinal autointoxication may even occur in cases in which the chemical composition and the colloid-chemical structure of the food are normal. On account of considerable individual differences observed, the origin of autointoxication is in the first instance thought to be dependent on the *vital capacity* of cells, tissues and organs.

Occasionally the condition of "conditioned intoxication" may be accompanied by the phenomenon of "conditioned deficiency" characterised by a shortage of blood components, e.g., copper, the composition of the food being normal in this

respect. Probably this observation reveals a new approach on the problem of different kinds of " pica," symptoms of " licking disease " (" lecksucht ")—if any—accompanying this condition.

It is important to notice that ions of minor elements may act as activators in enzyme reactions and that they may be taken up in the molecules of enzymes, vitamins or hormones, these complexes acting as catalysers in metabolic processes.[1]

It is especially the detoxication of endogenous poisons which offers a basis for a rational therapy by furthering oxidation of endogenous toxins, e.g., " diamines " (histamine) and phenols by means of minor elements (Co, Cu). It is a matter of fact that the addition of other suitable redox-systems showing an E_o value adapted to the animal tissues, e.g., methylene blue, may act in a similar way. The therapy using methylene blue is based on this observation.

A particular form of autointoxication, viz., ketonæmia in cattle of hormonal and alimentary origin, may be successfully controlled by treatment with ammonium lactate by mouth.

The observation of interference with autonomic nervous system makes the complex of biochemical and clinical features for the greater part intelligible.

The chemical disturbances of the blood in cases of autointoxication offer a basis for a therapy using magnesium ions, subcutaneously administered. Moreover, they explain why the intravenous administration of calcium is not advisable in these cases.

Conclusion

In conclusion we may point out that the results obtained concerning the nature, pathogenesis, prophylaxis and causal therapy of autointoxication in relation to food still show numerous gaps with regard to our understanding of these problems. To unravel the problems mentioned further research will be needed; in the first instance, to establish the biochemical nature of the specific toxins acting in the different metabolic disorders.

Summary

1. Owing to abnormal processes in the intestine, disturbances of absorption and abnormal metabolism of nutrients, a " conditioned intoxication " occasionally accompanied by " conditioned deficiency " may arise. This may even happen in cases in which the chemical composition and the colloid-chemical structure of the food are normal. Probably the mode of reaction of the animal body on the food administered is greatly dependent upon the *vital capacity* of the animal tissues and organs.
2. A particular condition of " conditioned intoxication " is shown to occur in alimentary ketosis when using as a fodder grass-silage containing much butyric acid. Administering lactate to these patients apparently makes up for the relative lack of this substance. It causes the symptoms of ketosis to disappear together with the fatty infiltration and degeneration of the liver and coprostasis.

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3. Clinical features such as intestinal obstruction, constipation, diarrhœa and "indigestion" (hæmorrhagic) enteritis, hæmoglobinuria, methæmoglobinuria, jaundice, paresis, staggering gate, tetany, excitation, sopor-depression, a frequent pulse rate, high temperature, rough coats, decreased intake of food, symptoms of dehydration and emaciation may point to this condition of *autointoxication*.

4. In all these cases the probability of interference with autonomic nervous system and with enzyme processes in which minor elements may play a part has to be taken into consideration.

5. In cases of gastro-intestinal disturbances in cattle and horses including the gastro-intestinal form of foot-and-mouth disease, and the gastro-intestinal form of founder (*pododermatitis*), considerable variations in individual values of minerals and organic substances in the blood were found. This is in accordance with the general nature of autointoxication phenomena, owing to considerable differences in the "intoxication-detoxication rate" in different animals.

6. In cattle there is an important point of similarity in the majority of cases observed. The calcium-phosphorus-magnesium rate of the blood serum is showing a shift in favour of inorganic phosphorus. This indicates that, as a rule, the "unfavourable" type of cardiac frequency curve following intravenous injection of calcium salts—so as to alleviate symptoms of paresis and tetany—is to be expected in the type of case mentioned. This is in accordance with the practitioners' experience.

7. In horses a hypomagnesemia—showing values down to 0.9 mg. per cent. of magnesium in the blood serum—occurs in the majority of the cases observed. In a series of cases of gastro-intestinal autointoxication, both in cattle and horses, fairly good results could be recorded from a *subcutaneous* administration of magnesium chloride in a 10 per cent. sterile solution.

8. An investigation of the nature of the toxic substances in cases of gastro-intestinal autointoxication in cattle and horses revealed the remarkable fact that very low histamine values of the blood often occurred. In horses the prognosis was unfavourable in these cases. Fairly good results were recorded in several cases by treating the animals by intravenous injections of methylene blue, showing a E_o value adapted to the animal tissues, so as to bring about an oxidation of histamine and other biogenic amines fixed in the tissues.

9. Experiments *in vitro* showed that from the minor elements observed it is cobalt which increases the rate of oxidation of histamine and cadaverine by the diamino-oxydase enzyme. However, in homogenous solution of blood serum this increase of the oxidation rate was shown to exist only at relatively high cobalt concentrations.

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A SURVEY OF BOVINE SALMONELLOSIS IN MID AND WEST WALES

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THE association of Salmonella organisms with disease in both adult cattle and calves has been reported from most parts of the world and has given rise to a somewhat voluminous literature.

In much of the early work on the disease, identification of the organisms was based on their biochemical characteristics, and because of this the identity of some of the organisms named must be accepted with reserve. With the development and application of accurate methods of determining the antigenic structure of members of the Salmonella group, later authors are in agreement that the organism most commonly responsible is *S. dublin*. *S. typhi-murium* is concerned to a considerably lesser extent, while occasionally other types, such as variants of *S. enteritidis*, are encountered.

There are very few references in veterinary literature to salmonellosis of cattle in Great Britain. Bosworth and Lovell (1931) and Craig, Davies and Massey (1941) have reported outbreaks of salmonella infection in calves, while John (1946), Bythell (1946), and Grunsell and Osborne (1948) have reported on salmonellosis in adult cattle.

Lovell and Hughes (1935) isolated *S. typhi-murium* from two out of a series of 100 calves examined bacteriologically in order to determine the cause of death. Both calves were approximately one month old. In 1931, Bosworth and Lovell described three outbreaks of *S. dublin* infection in calves. The first and third of these outbreaks occurred in batches of calves purchased by the Institute of Animal Pathology, Cambridge, for experimental purposes. The first outbreak affected calves between 2-3 weeks of age. Several appeared ill a few days after arrival and within a short time all were affected. The period of illness lasted from two to four days and there were 18 deaths and two recoveries. The early stages were characterised by dullness, inappetance and fever, followed by acute offensive diarrhœa, occasionally blood-stained, with evidence of abdominal pain. A number developed pneumonia. Shortly before death, the temperature fell to subnormal.

The third outbreak occurred in a further batch of 10 calves obtained for the Institute some months later from the same source. The authors regarded this as an extension of the first outbreak rather than a separate one. Eight of the 10 calves died.

The second outbreak affected primarily a bunch of three-weeks-old calves bought in the open market, but the disease spread afterwards to a number of home-bred animals ranging in age from 3-12 months. There were 17 cases and three deaths.. In these cases there was definite evidence of pneumonia but diarrhœa was not observed in any of the affected animals.

In 1941, Craig, Davies and Massey investigated an outbreak on a Cheshire dairy farm where losses had occurred among the calves for some years and found it to be due to *S. dublin*. On an average, about 20 per cent. of the calves were lost each year. Calves usually developed symptoms during the first 2-3 weeks of life, but occasionally not until 4-8 weeks. One calf examined had been ill for a month. Samples of blood and fæces were collected from adult cows in the herd and samples of milk from the cows in-milk, in order to determine whether any members of the herd were carriers of the infection. No Salmonella organisms were isolated from the fæces or milk. Agglutination tests were also carried out using both flagellar and somatic antigens of *S. dublin*, but it was concluded that the balance of evidence pointed to the absence of carriers among the adult cows.

John (1946) reported the isolation of *S. dublin* from cases of acute enteritis in adult cattle occurring in his practice in Carmarthenshire. Cases had been encountered for a number of years, but no specific diagnosis had been possible until fæces from affected animals were submitted to bacteriological examination. Cases were reported as being sporadic in character, usually one member of a herd being attacked, although occasionally more than one animal might be affected concurrently. Following John's report, Bythell (1946) described outbreaks of salmonellosis on two dairy farms in the West Midlands. On the first farm, 10 in-calf heifers or cows in a Shropshire herd of Dairy Shorthorns died during the autumn of 1945. None of the 10 cases appeared concurrently, the shortest interval between any two cases being one week. During the summer of 1945, six in-calf heifers were bought from South Wales. It was suggested that these animals may have introduced the disease. One of the six died within a month of arrival, a second aborted three months after arrival, and a few days later the first of the home-bred animals became affected. All the affected animals died. Blood samples from the adult cattle in the herd were submitted to an agglutination test against a *S. pullorum* somatic (0) antigen. Sixty animals had titres of 1/20 or less. Two had titres of 1/320, but neither had a history of previous illness. The fæces of these animals yielded *S. dublin* on culture.

The second outbreak occurred in a Friesian herd in Staffordshire. Two animals were affected at an interval of over two months. Both died. The examination of blood samples from this herd failed to show that any adult animal had a significant titre to *S. pullorum* and fæces samples from five animals showing the highest titres were negative for *S. dublin*.

More recently, Grunsell and Osborne (1948) have reported *S. dublin* infection in adult cattle on five farms in the Glastonbury area of Somerset. Seven animals were affected and two died.

It is clear, therefore, from a survey of the various reports, that *S. dublin* is responsible for losses in both adult cattle and in calves in this country. *S. typhi-murium* and *S. enteritidis* may also be concerned to a lesser extent. Data as to the relative incidence of disease associated with these organisms in Great Britain are, however, lacking, and this may be attributed, at least in part, to the fact that the bacteriological study of acute enteric infections in cattle in this country has been neglected.

Outbreaks of food poisoning among the human population have been traced to infected cattle. In the majority of outbreaks, the source of the infection has been contaminated milk. In some cases, the milk has come from herds containing clinically affected animals; in others, from herds containing healthy carrier animals.

McAllan and Howie (1932) described two outbreaks of milk-borne food poisoning in Aberdeen. *S. enteritidis* was identified as the cause of illness in 19 people, and also as the cause of enteritis in a cow suffering from persistent diarrhœa. The outbreak ceased with the removal of the cow from the dairy herd supplying the suspected milk. In the other case, *S. typhi-murium* was isolated from two human beings suffering from enteritis. One of the affected people had been nursing a recently purchased cow ill with profuse diarrhœa, from whose fæces *S. typhi-murium* was also isolated.

The same authors record an outbreak of acute enteritis occurring in Aberdeen in 1925. In all, 497 persons were affected and one died. The outbreak was traced to one dairy herd and to one cow in the herd suffering from mastitis. The organism, *S. enteritidis*, isolated from the udder and flesh of the cow, corresponded to the strain isolated from the human patients (see also Kinlock, Smith and Taylor, 1926).

Two outbreaks traceable to cows suffering from clinical disease have recently been reported in the *Lancet* (Anon 1947a, 1947b). The first outbreak occurred on September 7, 8 and 9, 1947, in the village of Kincardine O'Neil, Aberdeenshire. Of a total population of approximately 200, 97 people, including the farmer who supplied the milk to the village, his family and farm workers, developed symptoms of vomiting, nausea, abdominal pain and diarrhœa. The symptoms lasted for 2-3 days; thereafter most patients recovered rapidly. There were no deaths. Investigation showed that the only common food was milk. A visit to the farm showed that a cow had fallen ill on September 5 and had died on the 7th. Post-mortem examination showed severe enteritis with advanced inflammatory changes in the small intestine. The herd consisted of 16 cows in milk. Another cow had been off her food and two calves had suffered from diarrhœa. Twenty-one specimens of fæces from various households showed *S. dublin*. Milk from the cows taken on September 5 and 6 showed the same organism. A sample of bulk milk on the 9th was negative. Material from the cow at *post-mortem* examination showed *S. dublin*. The organism was not obtained from the fæces of any other cow but was recovered from the fæces of both calves.

The second outbreak occurred in the village of Little Houghton, Northamptonshire. Of a total population of 416, 133 people were affected, mostly on September 27 and 28, 1947. There was one death. Specimens of fæces from three patients on September 29 showed *S. dublin*. The milk was supplied from a single farm to all but 25 residents, none of whom became ill. Inquiry showed that on September 25 a prematurely calved heifer had been suspected of having a chill. Milk from this animal was not included in the milk supply after the 26th. The animal died on the 27th but the carcase had been disposed of by the time the knackery was visited. Samples of milk taken on the 28th and 29th were negative for Salmonella organisms. On September 30, samples of milk and fæces from each remaining cow in the herd were negative for Salmonella. Although the evidence in this outbreak was not conclusive, the circumstantial evidence clearly pointed to the sick cow as the origin of the outbreak.

Conybeare and Thornton (1938) described an outbreak of gastro-enteritis in Wiltshire involving over 100 persons, chiefly schoolchildren, associated with *S. dublin* and traced to one apparently healthy cow excreting the organism in the fæces. The affected animal was detected by testing the sera of all the milking cows for agglutinins to *S. dublin*. Two cows were found to have titres considerably higher than the other members of the herd. *S. dublin* was recovered from the fæces of one of these animals.

Tulloch (1939) recorded two milk-borne epidemics occurring in Dundee and both associated with *S. dublin*. In the first outbreak there were 373 known cases, and the source of the infection was found to be the milk of an affected cow. The second outbreak involved some 280 persons and was traced to another cow on the same farm.

Sutherland and Berger (1944) reported an outbreak of gastro-enteritis in the West Riding of Yorkshire. In all, 162 persons were affected. *S. dublin* was isolated from a sample of milk and from the fæces of seven patients. Cultural examination of individual milk samples from the suspected herd proved negative for Salmonella. An agglutination test of the whey from each cow revealed one apparently healthy animal with a whey titre of 1/32 to 1/64. *S. dublin* was recovered from the fæces of this animal. Rankin and Slavin (1947) subsequently kept this cow under observation for seven months. During the observation period, the fæces were examined periodically for *S. dublin;* except for one occasion, they were invariably positive.

A survey by Savage (1920) of outbreaks of salmonellosis over a number of years records at least seven outbreaks probably directly due to infection of the milk from a sick or carrier animal.

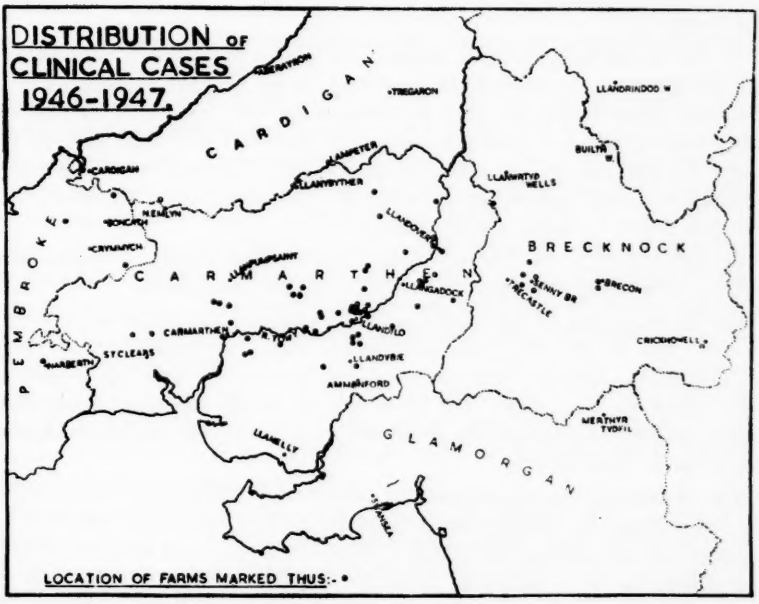
It is clear, therefore, that cattle both during the clinical stage of illness and in the carrier state are a potential source of danger to public health, outbreaks of food poisoning due to both *S. dublin* and *S. typhi-murium* having been traced directly to sick or carrier animals.

The Incidence of Bovine Salmonellosis in Mid and West Wales

Following the report by John (1946) that salmonellosis of adult cattle had

been diagnosed on a number of farms in his practice, an attempt has been made to obtain as accurate an estimate as possible of the incidence of this disease among the cattle population of West Wales. During the early stages of this investigation, observations were confined to that part of Carmarthenshire in which the disease had already been recognised, but were later extended to cover the whole of the Aberystwyth Advisory Province, i.e. the counties of Cardigan, Montgomery, Radnor and Brecon, together with parts of the adjoining counties of Carmarthen and Pembroke.

Veterinary surgeons were asked to submit material from clinical cases of disease in cattle showing symptoms similar to those described by John. Samples



of blood and fæces were asked for from all cases. A request was also made for samples of milk from affected adult lactating cows. The examination of such material has formed the basis of this survey. A number of veterinary surgeons in the Carmarthen area have submitted material from clinical cases to the Carmarthen Public Health Laboratory, which is directed by the Medical Research Council for the Ministry of Health. The medical members of the staff have been particularly interested in the problem of salmonella infection in cattle because of its importance in relation to public health, and they have assisted the writer by supplying a copy of all reports on the examination of material from suspected clinical cases in bovine animals. The positive reports from this source have been incorporated in the results presented.

Results

The general incidence of salmonella infection in cattle.—The results presented refer to the complete two-year period from January, 1946, to December, 1947, inclusive. During this period cases of salmonellosis in cattle have been diagnosed on 70 farms.

On two of the farms the initial investigation was concerned with the disease in calves of from 14 days to 3½ months of age. Further inquiry on one of these farms showed that a number of adult cattle had suffered from a clinical attack of salmonellosis some 15 months previously. It was possible to relate the disease in the calves to the presence in the herd of a number of the previously affected adult cattle. These animals, although recovered from clinical illness, were shown to be chronic carriers of infection and to be constantly excreting the organisms in the fæces.

In the second herd, cultural examination of the fæces and a serological test of the blood serum was carried out from each of the 79 adult animals. The herd had recently been established and, in consequence, the previous history of many animals was not known. The examination of the blood and fæces samples failed to show the presence of any adult carrier animals. The source of the infection in the calves was therefore not determined. On both farms, the illness in the calves was due to infection with *S. dublin.*

On another farm the affected animals were approximately 9 months of age; two died. The causal organism was identified as *S. typhi-murium.*

On the remaining 67 farms, the animals primarily affected were all over one year old. The oldest animal was a Hereford cow of approximately 14 years of age. This animal had given birth to her eleventh calf a few days before developing clinical symptoms of disease. On 64 of the 67 farms, specimens from affected animals yielded *S. dublin;* on the remaining three farms, the causal organism was found to be *S. typhi-murium.*

The number of animals affected on each farm.—Much of the data relating to individual outbreaks is, unfortunately, incomplete. In a number of cases veterinary surgeons have been content to submit material from one case only for diagnosis. Samples have not been submitted from other animals affected concurrently or at an interval following the primary case, such cases being accepted as salmonellosis if the first sample submitted to the laboratory was positive. The writer has, however, made personal observations on a number of farms over a period of two years. On the basis of these observations, together with information gained from veterinary surgeons and from the examination of material in the laboratory, a reasonably accurate picture of the number of animals involved on individual farms has been obtained.

A distinction has to be drawn between cases occurring directly associated with the primary infection and what may be termed secondary cases occurring after a considerable period of time. An example of the first type of case is that of two heifers concurrently affected three weeks following a case in an old cow, while an extreme example of the second type of case is that of a Friesian heifer brought into a herd in which carrier animals were known to be present and in

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which the last clinical case had occurred 21 months previously. The heifer developed clinical symptoms of salmonellosis three weeks after arrival at the farm.

The present observations refer only to the 68 outbreaks affecting cattle over 9 months of age. On 50 of these farms, only one animal is known to have developed clinical symptoms. On 11 farms, two animals were affected at intervals. The shortest recorded interval between the two cases on any one of these farms was 13 days and the longest interval 26 days. On one farm, two animals developed clinical symptoms concurrently. Two animals on another farm developed clinical symptoms concurrently 21 days after a primary case. In another outbreak, a primary case was followed at intervals by three further cases; and in another the primary case was followed by two further cases at intervals of 13-14 days. Other outbreaks recorded include one in which two animals were affected concurrently followed by two further cases the following day; and another in which a primary case was followed by the simultaneous development of symptoms in four heifers after an interval of two months.

It is evident, therefore, that whereas on the majority of farms cases are sporadic, only one animal being affected, on a number of farms several animals may be affected either concurrently or at intervals. The type of secondary case previously mentioned, occurring at a considerable period of time after the primary cases, is comparable to residual infection occurring in calves.

The ages of affected animals.—The ages of 39 of the affected animals have been obtained. Three of the animals were between 12 and 24 months of age, 15 between 2 and 4 years, 10 between 4 and 6 years, eight between 6 and 8 years, and three animals between 8 and 14 years. It is clear, therefore, that adult animals of all ages may be affected.

Breed incidence.—Cases have been diagnosed in cattle of the Welsh Black, Hereford, Ayrshire, Friesian, Shorthorn, Jersey and Red Poll breeds, as well as in various crossbred animals. The disease therefore affects cattle of all breeds likely to be found on Welsh dairy farms.

Sex incidence.—No case has been diagnosed in an adult bull. One case only has been diagnosed in a bullock. The remainder have all been heifers or lactating cows. This may be purely coincidental and related to the fact that the farms from which samples have been received are of the dairying and not the store, rearing type.

Mortality rate.—The information relating to cases occurring in 1947 is more complete in many essentials than that available for 1946. The assessment of the mortality rate in affected animals over one year old is therefore based on the data collected during the year 1947. Of 50 affected cattle, it has not been possible to determine the fate of 10 animals. Of the remaining 40 cattle, 29 (72.5 per cent.) animals died and 11 (27.5 per cent.) recovered. While these figures represent the total mortality rate, the death rate on individual farms has shown considerable variation. For example, all three affected animals on one farm died, while on another farm, of four affected animals, three recovered.

Seasonal incidence.—With the emphasis on winter milk production, dairy farmers attempt to arrange their breeding programmes so that the majority of the

cows calve in the autumn or early winter. In consequence, it is usual to find the largest number of young calves on a dairy farm in early winter. Each of the two outbreaks of *S. dublin* infection in calves occurred in the period from September to January. As the outbreaks in the calves may therefore be considered as special cases, they are omitted from Table I. In this table the primary cases of infection occurring on individual farms are shown under the month when symptoms were first noted. This table indicates that, while occasional cases were found in other months, the greatest number occurred during the period June-October inclusive, i.e. during the warmer months of the year. Of the 39 outbreaks recorded in 1947, 32 (82 per cent.) occurred during the months of July-October inclusive.

TABLE I.

Monthly incidence of outbreaks of salmonellosis in cattle during the years 1946-47 *in South-West Wales.*

(These figures refer to the first case to occur on each farm)

	Jan.	Feb.	Mar.	Apr.	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.	Total
1946 ...	1	–	1	1	2	6	5	3	6	2	2	–	29
1947 ...	2	–	–	–	1	3	8	10	6	8	1	–	39

Geographical Distribution of Outbreaks

A map is appended (Map 1) of the counties of Carmarthen and Brecon together with portions of Pembroke, Cardigan and Radnor. On it the positions of 68 farms on which cases of salmonellosis occurred during 1946-47 have been marked as accurately as possible. Reference to this map indicates that the following number of outbreaks were diagnosed in the various counties:—

	Cardigan	Pembroke	Carmarthen	Brecon	Total
Number of outbreaks ...	2	4	53	9	68

Approximately 80 per cent. of the cases, therefore, occurred on farms in the County of Carmarthen.

Description of the Disease

The following description of salmonellosis applies to the disease as it has been seen in cattle of different ages. There appears to be no essential difference between the symptoms exhibited whether infection is due to *S. dublin* or *S. typhi-murium*.

Clinical Symptoms

1. *Cattle under 1 year of age.*—Calves have been found to be affected with a salmonella bacteræmia during the first 2-3 days after birth. Affected calves were strong at birth and apparently healthy. For the first 24-36 hours they suckled well. About 48 hours after birth the calves became dull, showed a reluctance to suckle, favoured recumbency and, weakening rapidly, died 3-5 days after birth. A *post-mortem* examination of a dead calf showed no macroscopic lesions but *S. dublin* was recovered from the heart blood, liver, lungs, spleen and the mesenteric lymphatic glands. Such cases have only been encountered in herds in which adult carrier animals of *S. dublin* were known to be present.

The majority of cases in calves have occurred in animals of 7-28 days of

age although affected animals have been found up to 3½ months old. The initial symptoms were dullness, inappetance and a febrile reaction with a temperature rise to 104-105 deg. F. The initial febrile reaction was followed in about 24 hours by the passage of fæces with the colour and consistency of putty and containing small clots and/or streaks of blood. In rather older animals (3-4 weeks) the fæces were more liquid in character and only careful examination showed the presence of blood. Affected animals rapidly became weak, favouring recumbency. The extremities were cold to the touch. Some remained on the ground for long periods refusing all food. In fatal cases, death occurred 5-7 days after the onset of symptoms. Examination of fæces and blood samples from other calves in the herds showed that some of these had been exposed to infection without developing clinical symptoms. *S. dublin* has usually been recovered from the fæces of such animals. A few affected calves showed enlargement of the carpal and tarsal joints. Even severely affected animals have recovered although enlargement of the joints persisted for many months after apparent clinical recovery. The agglutinins in the serum of calves disappear at a variable rate. In calves recovered from the clinical disease, the disappearance of agglutinins has seemed to be closely related to the severity of the clinical symptoms; if the symptoms were severe, the agglutinins persisted for a longer period than in subjects with a milder train of symptoms and were still present at one year old. In calves exposed to infection but not developing clinical symptoms, agglutinins disappeared quickly and were no longer demonstrable 2-3 months subsequent to exposure to infection. ***As judged by the examination of fæces, calves of this age, recovered from clinical infection, do not remain carriers of the organism.***

A more chronic form of *S. dublin* infection has been seen in calves of approximately six months of age in which the only symptoms noted were lack of condition and diarrhœa, the fæces again being putty-like in consistency but not containing blood. The affected animals remained unthrifty for 1-2 months but eventually recovered. Subsequent examination failed to reveal *S. dublin* in the fæces of these animals.

Two animals of nine months of age in another herd died after showing symptoms of salmonellosis characteristic of the disease in older cattle. As a description of the disease as it has been seen in cattle over one year old follows, it is unnecessary to describe the symptoms seen in these cases.

2. *Cattle over 1 year old.*—Symptoms in adult cattle have been remarkable for their consistency, the main variation noted being in their severity. The common syndrome has consisted of an initial febrile reaction with the temperature varying between 104-107 deg. F., acute depression, generally complete inappetance and, in the case of lactating cows, complete or almost complete cessation of milk yield. During this stage the organism can be recovered from the blood. Evidence indicates that the organism is also present in the milk. This febrile stage is followed in 12-18 hours by the sudden passage of clots of blood in the fæces, merging gradually within a further 12 hours into a profuse fetid dysentery. In some cases the dysentery may not be preceded by the passage of blood clots. This is the stage generally seen by the veterinary surgeon by which time the temperature is usually

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2-3 deg. lower than in the initial febrile stage. At this stage also the organism may not be recoverable from the blood and the milk, but can always be recovered from the fæces. The dejecta invariably contains shreds of fibrin and in some cases of mucous membrane. The temperature falls to normal or sub-normal. In severe cases death may occur within 24 hours of the onset of symptoms. In prolonged cases there is rapid dehydration and emaciation. Resorption of the peri-orbital fat results in the marked retraction of the eyeball. The conjunctival mucous membrane is congested and icteric. Symptoms of abdominal pain are pronounced, the animal constantly turning its head to the flank and kicking at the abdomen. Affected animals become recumbent and comatose. The majority die within 24 hours to five days of the onset of symptoms. Occasional animals survive up to 14-16 days: they become a pitiful sight. Recovery is infrequent and apparently bears no relation to the severity of the symptoms. The agglutinating titre of the serum of affected animals in the first few days of the clinical disease is within the normal range of agglutinins to *S. dublin*. The blood titre rises during the course of the disease and reaches a titre which may be regarded as positive by the end of the first week of illness. These observations have been confined to agglutinating titres to *S. dublin*. It is not known whether a similar reaction occurs in infection with *S. typhi-murium*. The first sign of eventual recovery is that the animal starts to pick at food. Fæces gradually return to normal consistency. The convalescent period is usually long, the return to normal condition taking several months. *All adult animals recovered from infection appear to remain carriers.* The greater number of affected in-calf cows abort, but abortion is not a constant feature. Occasionally an animal may show a febrile stage of the disease only. In such cases the symptoms of a high temperature, cessation of milk yield and depression subside after a short course of approximately 24 hours. Such transient infections do not stimulate the production of anti-bodies. Occasionally also there may be an apparent lag phase between the febrile stage and the development of gastro-enteric symptoms. In one case an animal showed a febrile stage and three weeks later an enteric stage. Whether these were both manifestations of the primary infection or whether the enteric stage was indicative of a new infection it is impossible to stay, but it would seem probable that they were both manifestations of a primary infection.

A small number of cases have shown rather milder symptoms in which dysentery and acute depression have not been so marked. Such cases have shown a high recovery rate after an illness lasting only 2-3 days. It has been noted, however, that even in-calf cattle showing such milder symptoms generally abort. Finally, animals may develop high agglutinating titres and the carrier state without having shown any clinical symptoms of disease.

Post-mortem Examination

A number of *post-mortem* examinations have been made on adult animals dying of a *S. dublin* infection. In all such cases the disease has followed its normal course, i.e., a primary febrile reaction followed by symptoms of gastro-enteritis. The following description of a representative *post-mortem* examination

serves to emphasise that in all cases the characteristic lesions are in the gastro-intestinal tract.

The lungs showed hypostatic congestion but the pleura was normal. Hæmorrhages were present on the apex of the heart wall and at the junction of the auricles and ventricles. The liver was enlarged, showed fatty degeneration and a cavernous hæmangioma. The mucous membrane of the gall bladder was inflamed and the bile thick. The rumen, reticulum, omasum and abomasum showed no macroscopic lesions.

In the small intestine lesions occurred at intervals throughout its length. Some areas appeared macroscopically normal. Other parts showed a muco-enteritis, while the greater portion showed an inflammatory reaction varying from petechial hæmorrhages to areas showing diffusely hæmorrhagic inflammation. The intestinal contents varied according to location, in some areas consisting only of mucous, while in others consisting of long shreds of bloodstained necrotic material. The large intestine showed similar variation in different areas. The longitudinal rougé were very pronounced and inflamed, varying from red to bluish-black in colour. Some of the mesenteric glands were enlarged and hæmorrhagic while others were œdematous only.

On culture *S. dublin* was isolated from the heart blood, liver, bile, spleen, intestinal contents and from milk, as well as from the mesenteric, ileo-cæcal and cœliac lymph glands.

Differential Diagnosis

There are several conditions in cattle with which salmonella infection may be confused and a differential diagnosis is therefore essential. Several of the cases diagnosed in the laboratory as salmonellosis during the course of this survey have, in fact, been diagnosed as one or other of the following conditions by veterinary surgeons.

(a) *Coccidiosis.*—There is a striking similarity in the seasonal incidence of coccidiosis and salmonellosis. In both conditions, although sporadic cases may occur throughout the year, the highest incidence is in the warmer months. Cases usually begin to appear in June, continue throughout he summer and disappear towards November. Thus, both diseases occur, in the majority of cases, in cattle at pasture and probably less than 5 per cent. of clinical cases are found in cattle kept indoors.

Coccidiosis generally attacks animals aged between four months and two years, being especially severe in animals 10-18 months old. It has been observed, however, in calves as young as four weeks and in cattle up to nine years old. Generally speaking. coccidiosis may be regarded as being enzootic among growing stock and sporadic only in adult stock. Salmonellosis affects cattle of all ages from birth to old age but the highest incidence appears to be in cattle of 1-4 years. There is therefore some similarity in the age incidence. In both diseases several animals may be affected concurrently.

The incubation period in coccidiosis varies, but the average is approximately

three weeks. In several recorded outbreaks of salmonellosis, secondary cases have occurred roughly three weeks following a primary case.

The symptoms and course of the infection are similar in both diseases. In both the first symptom noted may be the passage of blood clots per rectum with straining and signs of abdominal pain, followed by a profuse offensive dysentery. Both conditions are characterised by rapid loss of condition, inappetance and, in the milking cow, cessation of milk yield. In both conditions death may occur within 24 hours of the onset of symptoms or the animal may eventually recover completely after a long convalescent period of unthriftiness. There are some slight differences in the location of lesions seen at *post-mortem* examination but both conditions are characterised by hæmorrhagic inflammation of the gastro-intestinal tract.

The two diseases, therefore, show such striking similarity that it may often be impossible in districts where both are endemic to make a differential diagnosis on clinical symptoms alone. A differential diagnosis can be made by the examination of the blood and fæces of affected animals. In coccidiosis, the oocysts may be demonstrated in the fæces on microscopical examination. In salmonella infection, the organism can be isolated from the blood in the early febrile stage of the disease and can always be isolated from the fæces in the enteric stage of infection.

(b) *Bracken poisoning.*—Poisoning by *Pteris aquilina,* the common bracken, has been observed in cattle, particularly in young stock, during the early autumn, from August to November. The symptoms are sudden in onset and are characterised by fever, dullness, loss of appetite, a bloodstained discharge from the nose and mouth and the passage of bloodstained fæces. The most characteristic lesions at *post-mortem* examination are petechial hæmorrhages in the alimentary tract and internal organs and under the skin.

The similarity in the seasonal incidence and symptomatology of bracken poisoning and salmonellosis has led to confusion and mistaken diagnosis in some cases. There is, in fact, little difference in the clinical picture, except that in salmonellosis there is no discharge from the nose and mouth. However, these are not constant findings in bracken poisoning. A differential diagnosis must depend upon an examination of the fæces of affected animals for salmonella organisms.

(c) *Chill.*—An outbreak involving a number of heifers and included in this survey was originally diagnosed clinically as a chill. The appearance of the disease in these animals coincided with a change of weather. It was not until some months later when losses occurred in calves secondary to the infection in the heifers that a systematic investigation led to the cause of the previous illness in the heifers being accurately determined.

A similar diagnosis of chill was made in the case of the animal incriminated as the starting-point of the outbreak of gastro-enteritis among the human population in Northamptonshire and reported in *The Lancet* (Anon, 1947b). Such a diagnosis is likely in cases showing a rather milder train of symptoms, i.e., cases in which the enteric symptoms are not pronounced and which make a speedy

recovery. A similar diagnosis might also be made in occasional cases showing a temperature reaction only, that is, cases of transient infection.

Protocols of Representative Outbreaks

Protocols of a number of representative outbreaks illustrate some of the differences in the nature of salmonella outbreaks as seen in a number of herds. Case No. 1, for example, illustrates the most common type in which only one animal in a herd develops clinical symptoms, while case No. 2 is representative of an outbreak involving a number of animals. Case No. 3 is an example of an outbreak involving calves.

Case No. 1.—An adult Shorthorn cow developed typical symptoms of salmonellosis in January, 1946, a few days after calving. An anærogenic strain of *S. dublin* was recovered from the fæces. After an illness lasting some seven days the animal gradually recovered.

Blood and fæces samples were taken from the 33 members of the herd in an attempt to trace the source of the infection. No animal in the herd except the affected cow had a blood titre greater than 1/160 and *S. dublin* was isolated from her fæces only. Blood and fæces samples have been taken from the recovered animal at intervals from April, 1946, to March, 1948, and an anærogenic strain of *S. dublin* has been isolated from the fæces on all occasions.

The calf of this animal, born in January, 1946, died when seven days old. The cause of death was not investigated. In January, 1947, the animal calved for a second time. The calf was allowed to suckle the dam and within two days had a temperature of 104 deg. F. and malaise. At this time the blood serum of the calf showed a flagellar (H) titre to *S. dublin* of 1/1280 and a somatic (O) titre of 1/160. An anærogenic strain of *S. dublin* was recovered from the calf's fæces. The calf recovered.

On December 18, 1947, a decomposing eight months fœtus was removed from this animal. It was estimated that the calf had been dead for approximately one week. The stomachs, intestine, liver and spleen of the dead fœtus were forwarded to the laboratory for examination. Anærogenic strains of *S. dublin* were recovered from the stomach contents, liver tissue and splenic pulp.

This case is an example of a herd in which only one animal is affected. The examination of the remainder of the herd failed to show a carrier cow which could have been responsible for infecting the sick animal. The case illustrates the persistence of infection in recovered animals; in this particular case the animal having remained a carrier for at least 26 months. Other points of interest are: (a) the high blood titre of the calf examined in January, 1947, due, as will be shown later, to the transfer of antibodies from dam to calf via the colostrum, and (b) the transmission of infection from the carrier dam both to this calf and to the one infected *in utero* in December, 1947.

Case No. 2.—Six maiden Shorthorn heifers were turned on to a hill to graze in the spring of 1946. The hill carried other stock and had a certain amount of bracken on it. In August one of the heifers developed acute diarrhœa, aborted a calf of about 10-12 weeks and died after an illness lasting seven days. The symptoms together with the presence of bracken in the alimentary tract led to a

diagnosis of bracken poisoning. During September, three of the remaining five heifers fell ill with similar symptoms. All three aborted calves of 3-4 months. All recovered after a few days' illness. *Thus all four affected animals aborted.*

Of the three recovered animals, one was sold. At the end of October, 1946, fæces and blood samples were taken from the four heifers remaining from the original six. The fæces were cultured and the blood samples submitted to an agglutination test with the following result :—

Animal	History	Blood titre of *S. dublin* "H"	Blood titre of *S. dublin* "O"	Culture of fæces
1.	Aborted in Sept., 1946. Symptoms of scouring, inappetance, etc., for a few days. Recovered.	1/163920	1/1280	*S. dublin*
2.	No symptoms seen by owner. Safely in-calf 4½-5 months.	1/81960	1/640	*S. dublin*
3.	Aborted Sept., 1946, at 4 months. Symptoms of scouring & anorexia. Fœtal membranes retained.	1/2560	1/640	*S. dublin*
4.	This animal had not aborted so far as the owner knew and was barren at examination. No history of acute illness.	1/10	1/10	*S. dublin*

It was in animals Nos. 1 and 3 that clinical symptoms had been noticed and abortion had occurred. No symptoms were seen in animals Nos. 2 and 4. As the animals were seen only once or twice weekly by the owner, however, an illness of short duration in animal No. 2 may have been missed. Alternatively, this animal may represent an atypical case, i.e., an animal in which the carrier state became established without the development of clinical symptoms.

On January 6, 1947, a *post-mortem* examination was made on an eight-day-old calf from this farm. It was strong when born and suckled well, but after some two days it showed a gradually developing lassitude and weakness and a reluctance to suckle. The dam occupied one half of the same double standing in the byre as one of the carrier heifers (heifer No. 2). No macroscopic lesions were seen at *post-mortem* examination but a bacteriological examination gave the following results :—

Material	*Culture* Desoxycholate citrate agar—direct	D.C.A. from Selenite broth
Lung—calf	*S. dublin*	
Heart blood—calf	*S. dublin*	
Liver—calf	*S. dublin*	
Bile—calf	*S. dublin*	
Spleen—calf	*S. dublin*	
Mesenteric lymph gland—calf	*S. dublin*	
Intestinal contents—calf ...	*S. dublin*	
Fæces—dam	Negative	*S. dublin*
Fæces—heifer No. 2	*S. dublin*	

There is no doubt that this calf died of a salmonella bacteræmia and that the infection was contracted from the infected adult cattle. In both cases No. 1 and 2, therefore, there is evidence that calves may become infected from adult carrier cows.

This outbreak illustrates :—

1. The high abortion rate in some outbreaks.
2. A type of outbreak in which enteric symptoms are relatively mild and of short duration with a high recovery rate.
3. The probability of transmission of infection from adult carrier cattle to calves.
4. The bacteræmic type of infection in calves.
5. The possibility of atypical cases giving rise to a healthy carrier state.

Case No. 3.—Case No. 3 refers to the disease in calves. This is an excellent example of an outbreak involving young stock and traceable to the presence of adult carrier cows in the herd.

The disease in the calves was not investigated until December, 1946. The owner reported that from September onwards the majority of his calves when 7-8 days old had developed a fœtid diarrhœa, the ejecta containing small clots of blood. Three calves had died. The herd had a similar history of losses in calves in the autumn and early winter of 1945. On December 18, 1946, samples of fæces from two affected calves were examined culturally and both yielded *S. **dublin***.

The previous history on the farm indicated that in August or September, 1945, several animals in a bunch of heifers grazing a meadow bounded by a river had developed a high temperature and diarrhœa. One animal died but the remainder recovered. The condition was diagnosed as a chill.

Blood and fæces samples were taken from all the animals in the milking herd on January 9, 1947. Because of the prevailing weather conditions, it was not possible to test the remainder of the cattle until March 21, 1947.

The result of the examination showed that seven adult animals had high agglutination titres to *S. **dublin*** and all were excreting the organism in the fæces. These animals were all in the age group, 3-4 years, and were members of the bunch of heifers which developed diarrhœa in the autumn of 1945. It is therefore probable that the illness in this bunch of heifers was due to a *S. **dublin*** infection.

Four additional adult animals had no significant blood titre but *S. **dublin*** was isolated from the fæces at this test.

Of the calves, two had high "H" (flagellar) and "O" (somatic) titres to *S. **dublin*** and positive cultures were found in the fæces. Two calves had high "H" titres but no "O" titre and *S. **dublin*** was present in the fæces, while *S. **dublin*** was also recovered from the fæces of two further calves with no serum agglutinins.

Subsequent tests showed that the significant animals from the infective point of view were the seven adult animals with high titres and excreting *S. **dublin*** in

the fæces. (See Table No. 2, Group 1 : Adults.) The remaining adult animals with *S. dublin* in the fæces at this test were negative on subsequent occasions. Not one of these animals had a significant titre to *S. dublin* so that it is unlikely that they had suffered from a clinical attack of the disease. It is possible that such animals represent contact carriers (Table 2, Group 2 : Adults).

All the calves positive on fæces examination subsequently became negative to repeated tests suggesting that calves either clear themselves of infection or that the organism localises in certain sites and is not excreted in the fæces. Several of these calves had passed through a clinical attack of the disease. The examination of these calves illustrates an essential difference between the disease in adult cattle and in calves, for whereas adult animals, recovered from the clinical disease, continue to excrete the organism regularly in the fæces, calves recovered from infection do not do so. (Table 2. Group 3.)

(*To be continued*)

TRICHOMONIASIS

The Breeding Record of a Bull over two years known to be infected with *Trichomonas Fœtus* (Str. Belfast)

By R. J. COOPER
Ministry of Agriculture, Northern Ireland

In March, 1946, a double dairy English Shorthorn bull was introduced into a herd containing 156 Shorthorn-type cattle of breeding age.

In this herd there had been a history of infertility during the previous 12 months. Trichomoniasis was suspected.

In April, 1946, an investigation was carried out, and of the 18 animals which were returning to service at that time, eight of them were tested. Seven of the animals were positive to the intradermal (Tricin) test and direct examination showed that two of them were excreting large numbers of trichomonads, whilst the blood of three was positive to the agglutination test. Infection with *trichomonas fœtus* (Str. Belfast) in the herd was thus confirmed.

The newly introduced bull had at this time served three cows, and, on being tested, he was found to be positive to the intradermal test and a normal saline washing from his sheath revealed trichomonads on microscopical examination.

In May, 1946, treatment of the bull was instituted on the following lines :—

Under epidural anæsthesia the penis was fully drawn, thoroughly washed with soap and warm water and bathed in a solution of hydrarg. perchlor. 1 : 1,000. The penis was allowed to dry and then covered with acriflavine emulsion. Subsequently, his sheath was irrigated every second day with a solution of hydrarg. perchlor. 1 : 2,000 and acriflavine emulsion introduced.

At the end of a month this treatment was discontinued and proprietary bull cones manufactured for this purpose were introduced into the sheath three times a week for a period of one month.

A resting period followed, and at the end of six months it was decided that,

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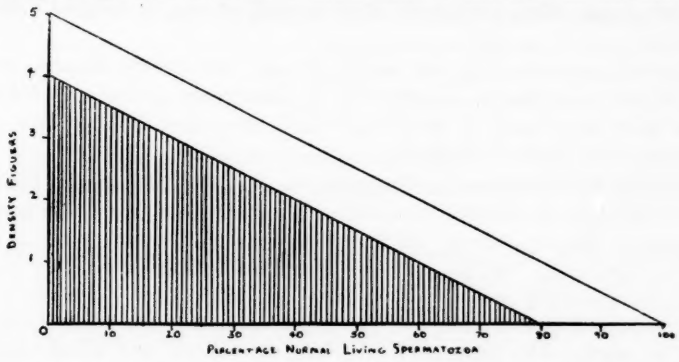
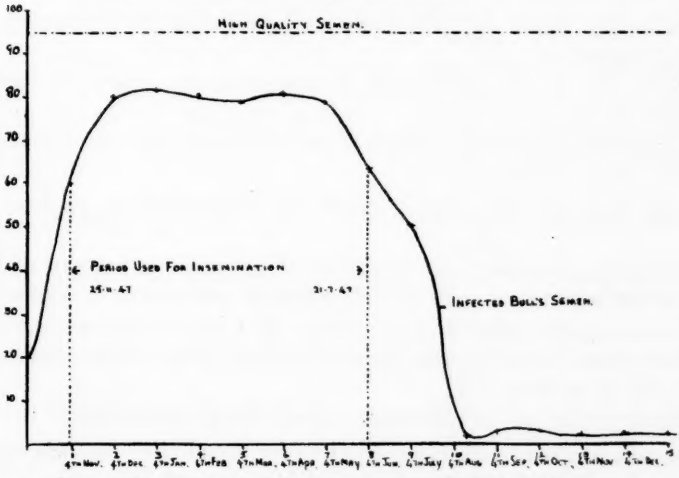
owing to the pedigree value of the bull, he should be used by the practice of artificial insemination in order to obtain some of his progeny.

The purpose of this article is to give the history of a trichomonad-infected bull during his period of artificial insemination. The bull at the end of two



years was slaughtered and *trichomonas fœtus* (Str. Belfast) organisms were found to be numerous in the preputial mucosa and the distal portion of the urethra. The penis appeared to be quite normal.

Graph Showing Quality Of Semen.



At no time, subsequent to his treatment and during his use for artificial insemination, was this bull allowed a natural mating.

Clinical History of the Bull

The evidence indicated that at the time this bull was introduced into the herd, trichomoniasis was present. He served three cows, one of which was subsequently proved to be infected.

Under epidural anæsthesia the penis was examined and the mucosa was

found to be acutely inflamed on the dorsal and ventral surfaces. There were a large number of pin-point zones of hæmorrhagic nodules which bled easily on being manipulated. This is the stage when bulls may exhibit what is commonly termed " lazy service." Another point which we have observed in this connection is that the penis, when withdrawn after natural service, is covered with small hæmorrhages.

After the treatment and rest period, already referred to, samples of semen were collected twice weekly, commencing on November 4, 1946. The first few samples were very poor in consistency and more than 50 per cent. of the spermatozoa were dead or abnormal.

The quality of the semen gradually improved until November 25, 1946, when he gave a satisfactory sample. The density of spermatozoa was fairly good, with approximately 90 per cent. of the sperms alive and showing good active progression. The semen was not used for inseminating cows after July 21, 1947, as it was deteriorating and considered unfit for insemination purposes, although samples were collected at intervals for examination for recording purposes in plotting a graph. On September 8, 1947, the sample was blood-tinged and contained some threads of a gelatinous material. There were no living sperms in the sample and thereafter the collections were very watery, containing only a few living sperms. Throughout the period in question, this bull always served vigorously.

The record of the quality of the semen is given in Graphs I and II.

The quality figure for the semen used in Graph II is assessed in the following manner :—

The density on the vertical axis is represented by colour and consistency varying from 0 to 5.

0 represents colour and consistency of a 3.92 per cent. solution of sodium citrate.

5 represents the rich creamy colour and consistency of the best quality semen.

1 represents the colour and consistency of a mixture of one part of the best quality semen added to 4 parts of 3.92 per cent. sodium citrate solution.

2 represents the colour and consistency of a mixture of two parts of the best quality semen added to three parts of 3.92 per cent. sodium citrate solution (and so on, up to four).

The horizontal axis is percentage normal living spermatozoa.

The area of the triangle mapped out by the points 0, 5, 100 thus represents the figure for the best possible semen and is designated 100.

From the density figure and the percentage normal living sperms, a triangle can be mapped out for any semen sample.

The semen quality figure for a sample of semen is taken as the percentage arc of the triangle 0, 5, 100, which the mapped out triangle for the particular sample represents.

For example, a sample of semen having a density corresponding to the

density figure 4 and containing 80 per cent. normal living spermatozoa, gives a semen quality figure of :—

$$\frac{\frac{4 \times 80}{2} \text{ (area of triangle 0, 4, 80)}}{\frac{5 \times 100}{2} \text{ (area of triangle 0, 5, 100)}} \times 100 = \frac{4 \times 80 \times 100}{5 \times 100} = 64$$

In a bull with a chronic trichomonad infection it would appear that there is developed some factor or factors which have a detrimental effect on the production of good quality semen.

Artificial insemination was commenced on November 25, 1946, and continued until July 21, 1947. The 40 animals inseminated were either cows which had not been mated subsequent to calving down normally or maiden heifers, and the following table gives their breeding records :—

No. of cow	Dates of Inseminations: first	repeat	Remarks
1. ...	25.11.46 ...	...	Proved in calf. Aborted at eighth month when suffering from *C. pyogenes* mastitis.
2. ...	3.12.46 ...	...	Proved in calf and calved normally.
3. ...	7.12.46 ...	...	Proved in calf and calved normally.
4. ...	7.12.46 ...	28.12.46; 28.1.47; 27.3.47 ...	Returned irregularly, showed a discharge — was treated and later proved in calf to another bull.
5. ...	7.12.46 ...	...	Proved in calf and calved normally.
6. ...	9.12.46 ...	16.12.46; 27.1.47; 3.3.47 ...	Returned at irregular intervals, treated and proved in calf to another bull.
7. ...	9.12.46 ...	...	Proved in calf and calved normally.
8. ...	14.12.46 ...	3.1.47; 3.3.47 ...	Returned showing a discharge after second insemination— was treated and proved in calf to another bull.
9. ...	14.12.46 ...	24.3.47 ...	Returned after three months and was treated.
10. ...	16.12.46 ...	6.1.47; 15.2.47 ...	Treated after first return and proved in calf to insemination on 15.2.47.
11. ...	16.12.46 ...	6.1.47; 18.2.47 ...	Proved in calf to third insemination and calved normally.

No. of cow	Dates of Inseminations: first	Dates of Inseminations: repeat	Remarks
12. ...	23. 6. 46 ...	14.1.47; 24.2.47 ...	Returned with a discharge, was treated and proved in calf to another bull.
13. ...	2. 1. 47 ...	18.2.47; 8.3.47; 28.5.47 ...	Returned showing a discharge. Treated and did not prove in calf to any bull.
14. ...	3. 1. 47 ...	Returned (on 7.2.47) ...	Returned and proved in calf to another bull.
15. ...	21. 1. 47 ...	3.3.47 ...	Proved in calf to second insemination and calved normally.
16. ...	21. 1. 47 ...	11.2.47; 8.3.47 21.4.47 ...	Returned at irregular intervals, was treated and proved in calf to another bull.
17. ...	25. 1. 47 ...	19.3.47 ...	Proved in calf to second insemination.
18. ...	28. 1. 47 ...	4.2.47; 6.3.47 ...	Returned with discharge, was treated and proved in calf to another bull.
19. ...	7. 2. 47 ...	Returned at two months ...	Returned at two months, was treated, but did not prove in calf to any bull.
20. ...	7. 2. 47 ...	...	Proved in calf and calved normally.
21. ...	19. 2. 47 ...	16.4.47 ...	Returned again, was treated and proved in calf to another bull.
22. ...	19. 2. 47 ...	...	Proved in calf and animal sold.
23. ...	19. 2. 47 ...	11.3.47 ...	Proved in calf and calved normally to second insemination.
24. ...	19. 2. 47 ...	...	Proved in calf and calved normally.
25. ...	24. 2. 47 ...	...	Proved in calf and calved normally.
26. ...	3. 3. 47 ...	27.3.47; 8.5.47 ...	Returned, was treated and proved in calf to another bull.
27. ...	3. 3. 47 ...	...	Proved in calf and calved normally.
28. ...	27. 3. 47 ...	23.5.47 ...	Returned showing discharge, was treated and proved in calf to another bull.
29. ...	27. 3. 47 ...	...	Proved in calf and calved normally.
30. ...	27. 3. 47 ...	...	Proved in calf and calved normally.
31. ...	31. 3. 47 ...	...	Proved in calf and calved normally.
32. ...	8. 4. 47 ...	16.5.47; 6.6.47 ...	Returned, was treated and eventually proved in calf to another bull.

33.	26. 4. 47	15.5.47; 10.6.47	Returned showing discharge, treated and proved in calf to another bull.
34.	26. 4. 47	27.6.47	Returned and proved in calf to another bull.
35.	8. 5. 47	Returned	Returned on 8.7.47 with discharge, was treated and eventually proved in calf to another bull.
36.	12. 5. 47	16.6.47; 8.7.47	Returned, treated and proved in calf to another bull.
37.	12. 5. 47	6.10.47 (Return date only)	Returned at over five months.
38.	12. 5. 47	31.5.47	Returned, was treated and eventually proved in calf to another bull.
39.	16. 5. 47	10.6.47	Returned, treated and eventually proved in calf to another bull.
40.	17. 5. 47	21.7.47	Returned at irregular intervals, was treated and did not prove in calf to any bull.

Breeding History Summary

Number of animals inseminated	40
Number of animals that proved in calf:	
First insemination	13
Second insemination	3
Third insemination	2
Number of animals that returned at over one month from first insemination	12
Number of animals which proved obstinate to treatment and proved sterile	3
Number of animals that returned, were treated and proved in calf to another bull	19

Summary

The breeding history of a bull known to be suffering from a chronic trichomoniasis is given.

This shows that a number of cows resisted infection in that they proved in calf.

The history of these artificially inseminated cows is in many ways similar to that found in cows mated normally to an infected bull, as it is well known

that many cows will prove in calf to a bull suffering from a mild form of the disease.

A number of animals were regarded as having become infected in that they exhibited the typical discharge and had passed the normal œstral period.

The two animals which returned at three months or over may be regarded as having aborted their fœtuses.

Acknowledgment

The author wishes to thank the Veterinary Research Division, Ministry of Agriculture, Northern Ireland, for their help and assistance in carrying out tests and examinations of samples.

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1948, July, Vol. 104, No. 7. Article :—Bovine Tuberculosis : Total Eradication as an Objective. A Review by J. T. Edwards, D.Sc., M.R.C.V.S., p. 230, line 33. *Delete:* (" exo-erythrocytic ").

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